ENVIRONMENTAL HEALTH ABSTRACTS & BIBLIOGRAPHY

April 1982

focus: LEAD POISONING

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL, ATLANTA, GEORGIA 30333

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Foreword

Environmental Health Abstracts and Bibliography presents a survey of recently published literature in the field. Effort is made to keep the abstracts as current as possible and sufficiently informative to enable the reader to decide whether the original article would be of interest to him or her. The journals in which articles originally appeared should be checked for reprint addresses. The Centers for Disease Control (CDC) is unable to supply reprints of articles cited in this publication.

In compiling these abstracts we use the National Library of Medicine's (NLM's) interactive retrieval service, MEDLARS II. Under this system, both foreign and domestic biomedical periodicals are searched for material dealing with or related to environmental health. We also use the libraries of Emory University, CDC, and other federal agencies. Abbreviations of periodical titles are those used by MEDLARS and listed in NLM's *List of Journals Indexed in Index Medicus.*

Future issues of *Environmental Health Abstracts and Bibliography* will be devoted to various environmental health topics. Individuals wanting to be placed on the mailing key to receive future issues as published should write to the Environmental Health Services Division, Center for Environmental Health, Centers for Disease Control, Atlanta, Georgia 30333.

Vernon N. Houk, M.D.
Director
Environmental Health Services Division

Contents

GENERAL

Is Low-Level Lead Pollution Dangerous?

D. Gloag. BR MED J 1980 Dec 13;281 (6255):1622-5.

From author's conclusions: The inferences drawn from the published work about children's susceptibility to the effects of modest concentrations of lead differ widely. One report concludes that there is probably no threshold for toxicity and that neurotoxic effects are liable to occur above a lead concentration of 5 ppm in dentine and 0.24 μmol/l (5 μg/100 ml) in blood. Another report concludes that there were toxic effects above 3.9 μmol/l (80 μg/100 ml) and that there was no convincing evidence of effects below about 1.7 μmol/l (35 μg/100 ml). Although the research findings are "somewhat contradictory," the evidence suggests slight cognitive impairment (an average of one to five points' reduction) and, possibly, behavioral difficulties as a result of persistently raised blood lead concentrations over 1.9 μmol/l (40 μg/100 ml); with concentrations below this, there are pointers to psychological risks, but the evidence is inconclusive.

Children and Lead: Some Remaining Doubts (Editorial)

Anonymous. ARCH DIS CHILD 1980 Jul; 55(7):497-9.

This editorial summarizes the conclusions of two comprehensive and authoritative reports on the effects of lead on the health and development of children. Although neither report conclusively confirmed a link between moderate body lead burdens (insufficient to cause obvious poisoning) and neuropsychological impairment, the majority of studies suggest such an adverse effect. Calculations suggest that the average city child derives 55%-95% of his blood lead from food, 0%-40% from water, and 3%-10% from air. Inhaled lead thus appears relatively unimportant. Priority should be given to removing lead-based paint from old houses, reducing lead in tap water in those areas where plumbosolvent water is drawn through lead pipes, and reducing emissions of lead into the air from gasoline.

Residual Effects of Lead Poisoning on Denver Developmental Screening Test Scores

S.C. Kirkconnell and L.E. Hicks. J ABNORM CHILD PSYCHOL 1980 Jun;8(2):257-67.

Authors' abstract: Subtest and total scores on the Denver Developmental Screening Test were examined for a group of 22 preschool-aged low-income children who had been lead poisoned, then medically deleaded. Pretest scores were obtained before blood lead elevations occurred; posttest scores were obtained an average of 4.5 months after deleading. Pretest scores were comparable with those of a matched control group, but posttest scores on the Fine Motor-Adaptive subtest declined, indicating significant residual effects of lead poisoning.

Some Comments on the 1980 Report of the United Kingdom DHSS Working Party on Lead in the Environment

M.J. Duggan. SCI TOTAL ENVIRON 1980 Dec;16(3):285-91.

A Department of Health and Social Security (DHSS) Working Party was appointed in 1978 to review the overall effects on health of environmental lead from all sources, particularly its effects on children's health and development, and to assess the contribution lead in gasoline makes to the body burden. Present author criticizes the Working Party's Report, which was published in March 1980, for a lack of emphasis on the exposure of children. The author is also critical of other aspects of the Report: "The Report does not deal with lead in dust and soil in a very unified way and plays down the importance of the contribution from petrol-derived lead by its emphasis on other sources—for example, paint, emissions from lead works, and such miscellaneous sources as the lead-based cosmetics used by the Indian community." The Report concludes that lead in gasoline is not an important contributor to the lead body burden in children and that the blood-lead level of this population is not high enough to give cause for concern. Author maintains that the Working Party, in reaching its conclusions, concentrated on adult rather than child exposure, and did not con-

sider data (from other countries) which suggest marked urban/suburban or urban/rural ratios for children's blood-lead levels.

Lead Poisoning: A Historic View

E. Morris. OCCUP HEALTH (LOND) 1980 Sep; 32(9):449-59.

From author's discussion: Of all the diseases known to medicine, few have been so widely studied and described as lead poisoning. Between the years 1500 and 1900 it reached almost epidemic proportions in many countries. The main symptom was severe, persistent abdominal pain, leading in many cases to eventual death.

A milestone in the gradual awareness of the harmful effects of lead was the investigation in 1767 by Sir George Baker of an ailment known as Devonshire Colic. Baker noticed an analogy between lead colic and Devonshire Colic, an ailment which frequently befell people who drank cider made in Devonshire, where it was common practice to line cider presses with lead. His findings were reported to the Royal College of Physicians, and, as a result, the practice of putting lead linings in cider presses was discontinued.

In 1839, a Frenchman, Tanquerel des Planches, conducted a very thorough study of lead poisoning. He showed clearly the causes and symptoms of such ailments, and later studies added little to his findings. The problem, however, lay not so much in the identification, but rather with the remedies. In the latter half of the 19th century, legislative attempts were made to overcome the problem of lead poisoning in industry.

Lead is a normal constituent of human tissue and regular absorption is a universal human experience. Only a small proportion of normally ingested lead is actually absorbed into the body. When an individual is exposed to more than the usual quantities of lead in the normal environment, evidence can be found in the body. Because specific clinical signs and symptoms do not usually present themselves until the stage of poisoning is reached, effective monitoring can only be done by using biochemical and hematological methods to determine changes before the onset of symptoms.

Absorption of Lead in Ancient Mesopotamia

P.B. Adamson. MED SECOLI 1979 Sep-Dec; 16(3):333-7.

Evidence has been presented that lead poisoning did occur in ancient Greece as early as the beginning of the fourth century B.C. Lead and silver ores were extensively mined in Anatolia and Armenia in antiquity. The most commonly mined lead ore in Asia Minor in antiquity was galena, an easily mined yet relatively nontoxic substance. Lead products were used in cosmetics in ancient Mesopotamia by both sexes. In view of the widespread use of lead in trade and industry and of colored lead salts for cosmetic purposes, it is surprising that cases of overt plumbism are not frequently mentioned in Akkadian literature, but this is not the case. Although inhabitants of Mesopotamia, Greece, and Rome were all exposed to toxic lead salts, the degree of plumbism must have varied markedly between these different societies. Mesopotamian burial practices, however, left skeletal material exposed to acid soils and subsurface water, so it is hardly surprising that the archaeologists concerned took neither skeletal long bones nor samples of the surrounding soil to be chemically analyzed for lead content. This situation may, however, be remedied in future archaeological explorations.

Psychometric Techniques in Environmental Research

J.A. Valciukas and R. Lilis. ENVIRON RES 1980 Apr;21(2):275-97.

Authors' abstract: Behavioral changes may be the earliest and only manifestation of neurotoxicity. Moreover, it is well known that extensive brain damage can occur with little or nondetectable clinical neurological deficit. Psychometric techniques now in use in toxicological and epidemiological research have been proposed to assess in an objective manner early manifestations of functional neurological changes that may be due to environmental neurotoxic agents. Methodological issues are reviewed and the following topics are addressed: (1) the description of representative examples of performance tests; (2) the validity and reliability of psychometric techniques; (3) the analysis of individual and composite test scores; (4) the nature of these variables; (5) the assessment of individuals and groups; (6) the use of multivariate statistical techniques; (7) the assessment of dose-response relationships; and (8) some methodological problems in the evaluation of neurotoxic effects when confounding variables are present. Psychometric techniques can be easily included in the protocol of cross-sectional health evaluation studies (morbidity studies); the sensitivity of psychometric techniques is partly a function of the discriminative selection of the appropriate tests, but it may be enhanced through the use of adequate mathematical-statistical techniques.

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*Valciukas JA, Lilis R: Psychometric techniques in environmental research. ENVIRON RES 1980 Apr; 21(2):275-97.

*Abstracted

SOURCES AND ETIOLOGY

Poisoning from Heavy Metals (Mercury, Lead, and Cadmium)

J.J. Chisolm, Jr. PEDIATR ANN 1980 Dec; 9(12):458-68.

From author's conclusions: Exposure of the family to heavy metals is primarily through dust, food, and, in certain locations, water. About half of present lead production and use is devoted to the manufacture of lead-acid batteries. In this usage, about 98% of the lead is recovered and recycled, while many of the remaining uses ultimately result in the dispersion of lead into the environment. However, the uses of cadmium and mercury result ultimately in the dispersion of 80% to 90% into the environment. All of these heavy metals ultimately come to rest in surface soil, aquatic bottoms, and sewage sludge. Thus, heavy metals can enter the home and its inhabitants in many ways. Maintenance of residential surfaces in good repair and cleanliness are clearly important in suppressing this type of contamination. Good industrial practice, which prohibits the transport of heavy-metal-containing dust on the clothing and person of workmen from the workplace to the home, would prevent this type of contamination. Mercury and lead readily cross the placenta. Outbreaks of severe poisoning have demonstrated their fetotoxicity. Cadmium apparently does not cross the placenta. Postnatally, once these metals are assimilated into the body, they are very slowly excreted. In industrialized societies, the body burdens of lead and cadmium increase with age. Fortunately, 90% or more of the total body lead burden is sequestered in bone. There is no evidence that it is released rapidly enough from bone to cause toxicity in the soft tissues late in life. Although chelation therapy may be lifesaving in acute inorganic mercury and lead poisoning, it does not necessarily prevent serious sequelae. The suspected benefits of chelation therapy in chronically increased lead absorption remain to be documented. In any case, therapeutic maneuvers cannot substitute for adequate preventive measures. Clearly, the only valid public health approach in the long run is the preventive approach.

Sources of Lead Pollution

D. Gloag. BR MED J 1981 Jan 3;282(6257):41-4.

From author's discussion: Environmental lead concentrations today are grossly increased over the natural levels, even far away from cities. An appreciable number of young children, and possibly pregnant women, may have undesirable concentrations of lead in their blood. A recent report concluded that most adult city dwellers not especially exposed to lead, and with blood concentrations in the usual range of 0.05-1.0 μmol/l (10-20 μg/100ml), derive 45%-90% of their blood lead from food, 0%-45% from water, and 10%-20% from air. In certain circumstances, inhaled lead might be the principal contributor. More tentative estimates for children are 55%-95% from food, 0%-40% from water, and 3%-10% from air, provided that no substantial amounts are ingested from paint, dust, or other sources. Another report proposes a range of 32%-69% for inhaled lead in adults. Considerable immediate benefits are likely to come from much more rigorous attention to the sources of lead thought to be important—especially industrial pollution, lead plumbing, lead paint, black spots for air pollution, contaminated dust and soil, and certain cosmetic preparations. More comprehensive monitoring of young children and pregnant women and of the environment, with investigations on the origins of environmental lead, could result in a large measure of protection.

Hair Lead Concentration in Children with Minimal Cerebral Dysfunction

J.C. Hansen, L.B. Christensen, and U. Tarp. DAN MED BULL 1980 Dec 6;27(6):259-62.

Authors' abstract: Lead concentrations in hair have been determined in a group of children with minimal cerebral dysfunction (MCD) and in a control group matched according to age, sex, socioeconomic level, place of domicile (rural or urban), and father's occupation. A significantly higher lead level was found in the MCD children compared with the control group. When compared with normal values reported in the literature, the lead levels in the hair of both groups could be regarded as within normal range. The role of lead as an etiologic factor in MCD is discussed.

Fecal Lead Excretion in Young Children as Related to Sources of Lead in Their Environments

P.B. Hammond, C.S. Clark, P.S. Gartside, O. Berger, A. Walker, and L.W. Michael. INT ARCH OCCUP ENVIRON HEALTH 1980;46(3):191-202.

Authors' abstract: Fecal lead excretion (PbF) was studied in young children with elevated lead exposure. PbB (blood lead concentration) was generally 40-70 μg/dl. The children's home environments were classified according to lead-based paint hazard and traffic density. There was a significant correlation between paint hazard classification and PbF but not between traffic density and PbF. There also was a correlation of PbB with paint hazard classification. Long-term fecal collections were instituted among 10 children who lived in high-hazard homes and 3 children with low PbB's, whose PbF's were considered normal. Among the children living in high-hazard homes, median fecal lead excretion generally was only moderately elevated. Grossly elevated amounts of lead were found only occasionally, and only in a few of the children. Movement of two children from a high-hazard home to a low-hazard home resulted in prompt and substantial reduction in PbF. By contrast, PbB fell only very slowly.

Blood Lead Levels of Some Children in New South Wales

A. Bell. MED J AUST 1981 Jan 10;1(1):23-6.

Author's abstract: The venous blood lead levels of 400 children under 16 years of age who lived in Port Kembla or in Cocklecreek and of 202 patients in several New South Wales hospitals are reported and compared with criteria announced by the National Health and Medical Research Council, the European Economic Community, and the American Environmental Protection Agency. The results of this study do not show reason for concern. The samples from hospital patients stress the importance of domestic exposure, such as to flaking paint containing lead. The findings of this study are also compared with a Victorian and a New South Wales survey of schoolchildren.

Ambient Lead Concentrations in New York City and Their Health Implications

B. Nathanson and H. Nudelman. BULL NY ACAD MED 1980 Nov-Dec;56(9):866-75.

Lead compounds are emitted into the atmosphere from three sources: gasoline-powered vehicles, industrial processes, and incineration. Lead compounds emitted by motor vehicles into the city's atmosphere are decreasing, but continue to outweigh all other sources. Data from rooftop samplers scattered around the city show, as expected, the highest ambient lead levels at stations closest to heavily traveled streets. The correlation between blood lead levels and these ambient measurements, although positive, does not appear to be very high. These data and evidence from the seasonal variation in lead levels suggest that insofar as the mechanisms of children's exposures are concerned, the total flux of lead into the environment appears to be more important than the concentration in any single primary or secondary medium of exposure or transport. The hypothesis that ingestion of deposited lead is the most likely pathway is reinforced by strong evidence to show that dust and soil lead can be significant determinants of blood lead levels.

A Fatal Case of Lead Poisoning Due to a Retained Bullet

V.J. DiMaio and J. Garriott. VET HUM TOXICOL 1980 Dec;22(6):390-1.

From authors' introduction: The most common causes of lead poisoning in the United States are ingestion of lead-based paint by children, consumption of "moonshine" liquor contaminated with lead, and environmental exposure. Lead poisoning from a retained bullet or missile is very rare and dependent on the location of the lead joint. Even rarer is death from lead poisoning due to a retained bullet. This case report describes a fatal case of lead poisoning due to a retained bullet.

Lead-Glazed Pottery: A Potential Health Hazard in the Middle East

A. Acra, R. Dajani, Z. Raffoul, and Y. Karahagopian. LANCET 1981 Feb 21;1(8217):433-4.

Authors' summary: Lead-glazed pottery produced by obsolete methods in Lebanon and other countries in the Middle East is potentially hazard-

ous when used in contact with acidic foods. This conclusion was deduced from the testing of 423 glazed utensils for the amount of lead leached by 4% acetic acid. Control measures, surveillance, and regulations are therefore warranted.

The Impact of Natural Radioactivity from a Coal-Fired Power Plant

A. Bauman and D. Horvat. SCI TOTAL ENVIRON 1981 Jan;17(1):75-81.

Authors' abstract: In a coal-fired power station burning coal which contained between 14-100 ppm U, ^{210}Pb was detected in the urine of an exposed group of individuals. Chromosome aberrations (complex, numerical, and the percentage of total aberrations) were also registered.

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Thomas HF: Domestic water usage and blood lead levels. PUBLIC HEALTH 1980 Sep;94(5):294-5.

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DIAGNOSIS AND SCREENING

What Happens in Lead Poisoning?

W.R. Lee. J R COLL PHYSICIANS LOND 1981 Jan;15(1):48-54.

From author's discussion: This article deals with some of the features of clinical lead poisoning. The subject is confusing, because much has been written, particularly in the occupational medicine journals, about the effects of increased lead absorption without the development of clinical symptoms. Quite a small intake of lead may produce detectable biochemical or even neurophysiological changes, and it is difficult, if not impossible, to decide when these changes are simply an adaptation to an increased intake of lead and when they indicate early poisoning. When a patient moves from symptomless "increased lead absorption" to lead poisoning, symptoms generally follow in a certain sequence. Lassitude is the first to appear, often followed by aching in joints and in limb muscles and by abdominal colic. Among biochemical changes is an increased urinary excretion of aminolevulinic acid and of coproporphyrin III. Motor nerve conduction velocity is often reduced, even in symptomless lead workers. The most frequently used diagnostic test for lead poisoning is the measurement of blood lead, which is limited by its poor discriminatory value. The most useful hypothesis for interpreting these results is to assume that the lead level in the circulating blood reflects not only the body burden of lead, but also the affinity for lead of the globin chains.

Laboratory Diagnosis of Lead Poisoning

S. Piomelli and J. Graziano. PEDIATR CLIN NORTH AM 1980;27(4):843-53.

From authors' introduction: Because lead poisoning in childhood is almost always the result of chronic exposure to lead, a laboratory diagnosis can usually be made long before overt clinical disease develops. It is important to detect childhood lead poisoning before it becomes symptomatic, since the neurologic syndrome has an insidious onset and then shows a sudden transition to overt and irreversible clinical intoxication. Additionally, the less obvious neuropsychological consequences that occur at lower levels of exposure can be prevented only if excessive lead intake is detected and the child is removed from the source of lead. Careful neurologic examination and the measurement of the blood lead level should allow early diagnosis. But the more subtle neurologic abnormalities are difficult to detect in any individual child, and, when the neurologic examination is clearly abnormal, it is usually too late to prevent permanent damage. Blood lead level is difficult to determine, expensive, and available only in highly specialized laboratories; moreover, both day-to-day variations in analytical results and environmental contamination of samples may diminish the reliability of the method. For these reasons, the diagnosis of lead poisoning rests, at least at the screening level, on the detection of abnormalities of heme synthesis, for which precise and extremely sensitive microchemical tests are available.

Lead Poisoning in Children

A.H. Drummond, Jr. J SCH HEALTH 1981 Jan;51(1):43-7.

The purpose of this article is to acquaint school health personnel with the dimensions of the lead poisoning problem. In a recent screening conducted by the Centers for Disease Control, some 7,950 of 116,668 children tested showed lead toxicity. In addition to these unsuspected cases, from 12,000 to 16,000 children are treated each year nationwide for lead poisoning; about 200 of these children die. Nearly all the tissues of a child's body are affected by lead poisoning, but the greatest effects are on the brain and nervous system. The early symptoms are often overlooked or misinterpreted. A correlation has been reported between blood lead levels and behavior, progress in learning, and level of ac-

tivity in outwardly normal children. Recent research suggests that there may be no safe threshold level of lead in a child's body below which there are no harmful effects. Several methods are recommended to detect children with lead toxicity and to reduce lead in the environment.

Riposte to "Environmental Lead and Young Children" (Editorial)

F.J. Coodin, C. Dawes, G.W. Dean, P.R. Desjardins, and J.B. Sutherland. CAN MED ASSOC J 1980 Sep 20;123(6):469-71.

In most environments it is difficult to determine the route of intake—inhalation or ingestion—of lead. Airborne lead may be inhaled or may settle on food and be ingested; lead in dirt may be ingested or may be resuspended as dust and inhaled. Children are not only more susceptible than adults to the deleterious effects of lead; but also, because of their physical characteristics and their tendency to put various objects in their mouths, children are likely to ingest more extraneous lead. A problem in the quantitation of lead pollution is the difficulty of accurately measuring blood lead levels. Because blood lead concentrations provide an indication of current or recent levels of exposure only, one investigator suggests measuring lead concentrations in bones or teeth to adequately assess the long-term effects of environmental lead exposure.

Impact of Community Screening on Diagnosis, Treatment, and Medical Findings of Lead Poisoning in Children

J. Schneider, B. Aurori, L. Armenti, and D. Soltanoff. PUBLIC HEALTH REP 1981 Mar-Apr; 96(2):143-9.

From authors' conclusion: Review of the medical records of 525 children diagnosed as lead poisoned during 5 years indicates that a citywide lead poisoning prevention program has resulted in a decrease in the number of children with lead-induced seizures and with central nervous system involvement, as well as a decrease in the mean whole blood lead concentrations (PbB's) in symptomatic children. However, the large number of multiple treatment episodes suggests a serious problem of re-poisoning because lead was not eradicated from the children's environments. The high proportion of children with PbB's of 40 μg/dl or greater indicates that the program has had a limited impact on the incidence of elevated blood lead levels. Findings of this study indicate that, although extensive screening and clinical follow up are effective in preventing the more serious aspects of lead poisoning, they do not address the issue of prevention.

Pica Patterns, Toxocariasis, and Elevated Blood Lead in Children

L.T. Glickman, I.U. Chaudry, J. Costantino, F.B. Clack, R.H. Cypess, and L. Winslow. AM J TROP MED HYG 1981 Jan;30(1):77-80.

Authors' abstract: Blood samples were obtained during a lead screening program from 100 children aged 1-6 years in Allegheny County, Pennsylvania, to determine whether there was any association between specific forms of pica and infection with *Toxocara canis*, the principal cause of visceral larva migrans in the United States, or elevated blood lead levels. Significant associations were found between: (1) feces, soil, or grass pica and *Toxocara* infection; (2) paint or plaster pica and elevated blood lead; and (3) dog ownership and *Toxocara* infection. These findings suggest that an accurate pica history may be useful in identifying potential health problems in children.

The Relationship between Zinc Protoporphyrin (ZPP) and "Free" Erythrocyte Protoporphyrin (FEP) in Lead-Exposed Individuals

V. Karacic, D. Prpic-Majic, and S. Telisman. INT ARCH OCCUP ENVIRON HEALTH 1980; 47(2):165-77.

Authors' abstract: The relationship between zinc protoporphyrin (ZPP) and total erythrocyte protoporphyrin, measured as "free" erythrocyte protoporphyrin (FEP), was determined in 194 adult subjects with different occupational and non-occupational lead exposures. Furthermore, the ZPP-FEP comparison was considered with respect to the dose-effect relationship of ZPP and FEP with blood lead (PbB) for males and females, respectively. Bilirubin (Bil.) interferences in ZPP analysis were taken into account. A very close and highly significant relationship ($r=0.962$, $p < 0.001$) was established between ZPP and FEP values. A significant correlation ($p < 0.001$) between log ZPP or log FEP and PbB (males, $r = 0.767$ and 0.718; females, $r = 0.525$ and 0.405) was also found. It was established, by both in vitro and in vivo studies, that Bil. interferes with the ZPP fluorescence readings; the relationship between "false" positive ZPP concentrations and Bil. concentrations (in vitro, $r = 0.987$; in vivo, $r = 0.903$) was highly significant ($p < 0.001$). A small but highly significant ($r = 0.948$, $p < 0.001$) influence of increased carboxyhemoglobin (COHb) concentrations on the decrease in hematofluorometer ZPP readings, due to inadequate oxygenation of the blood, was found. The results obtained confirm the usefulness of ZPP determinations using hematofluorometers for surveillance of in-

creased lead absorption but stress that the interfering effect of Bil. and, to a lesser extent, of COHb cannot be ignored.

Measurement of Near-Normal Concentrations of Erythrocyte Protoporphyrin with the Hematofluorometer: Influence of Plasma on "Front-Surface Illumination" Assay

R.B. Schifman and P.R. Finley. CLIN CHEM 1981 Jan;27(1):153-6.

Authors' abstract: Zinc protoporphyrin in erythrocytes increases in iron depletion. Because the hematofluorometer directly measures zinc protoporphyrin in whole blood, it may therefore be a useful screening instrument for detecting iron deficiency. We evaluated its performance with normal to slightly above-normal zinc protoporphyrin concentrations (0.2 to 2.0 mg/l) in erythrocytes, because this is a critical range for differentiating normal and iron-deficient individuals. There was excellent correlation ($r^2 = 0.900$) between erythrocyte protoporphyrin as measured by an extraction procedure and as measured directly with the hematofluorometer. However, at these concentrations, plasma caused hematofluorometer readings to be spuriously high, by 2.4% to 89.4%, an effect due to the instrument's optical design. The effect can be eliminated by washing the cells free of plasma or by allowing erythrocytes to displace plasma by settling to the illuminated surface before the measurement. The interference does not affect the hematofluorometer's sensitivity, but abnormal results obtained for whole blood should be confirmed with more specific tests, and interlaboratory precision may be influenced if whole-blood samples are used. A 1-min delay from sample placement to measurement decreased zinc protoporphyrin values by 2.6% to 36.9%. We also describe the use of cryopreserved control erythrocytes, for which the CV is 2.3% for a concentration of 0.96 mg per liter of erythrocytes, which are not affected by time of measurement and which are stable for 3 months.

Use of Magnetic Circular Dichroism Spectroscopy for Biologic Monitoring of Occupational Exposures to Toxicants

E.R. Zygowicz, B.R. Hollebone, and H.M. Perkins. CLIN CHEM 1980 Sep;26(10):1413-8.

Authors' abstract: Zinc protoporphyrin is the predominant fluorescent porphyrin accumulating in erythrocytes as a result of chronic lead absorption or iron-deficiency anemia. Although diagnostic concentrations or thresholds for it in erythrocytes have been inferred, normal adult averages have not been established. We quantitatively assessed average zinc protoporphyrin values during an investigation into the usefulness of magnetic circular dichroism spectroscopy as an analytical technique for biologic monitoring of industrial toxicant exposures. Blood samples drawn from 55 employees not exposed to lead were analyzed for blood lead, hematocrit, and zinc protoporphyrin. Average concentrations of zinc protoporphyrin determined with a hematofluorometer were compared with results obtained by magnetic circular dichroism spectroscopy. The latter results were comparable in kind but superior in quality to those of fluorometry. The magnetized spectroscopy followed Beer's Law at concentrations well below indigenous concentrations and was more sensitive than difference spectroscopy. Spectroscopic resolution of heme and zinc protoporphyrin moieties in a pyridine/NaOH mixture was complete.

The Determination of Free Erythrocyte Porphyrins (FEP) by a Semi-Automated Fluorometric Technique

J.J. La Brecque. ACTA CIENT VENEZ 1978; 29(6):479-81.

Author's abstract: This paper describes the adoption of a proportional pump scheme to automatically re-extract porphyrins from the original ethyl acetate-acetic acid solutions into HCl and to continuously determine the amounts of porphyrins in these solutions by a spectrofluorometer. The free erythrocyte porphyrins (FEP) determined by this method are compared with the results of the manual method and are also correlated with blood level measurements. [This semi-automated technique is rapid and can determine the FEP for about 40-50 samples per hour. The method is ideal for mass screening purposes and will detect lead poisoning, iron deficiency anemia, and other rare diseases.]

Direct Methods for the Determination of Lead in Whole Blood by Anodic Stripping Voltammetry

S.W. Lee and J.C. Meranger. AM J MED TECHNOL 1980 Dec;46(12):853-7.

Authors' abstract: Two methods for the direct determination of lead in whole blood by anodic stripping voltammetry (ASV) are described. The procedure in both methods involved the mixing of micro blood samples with a metal releasing reagent, Metexchange, and electrochemical analysis using carbon electrodes. A multiple Anodic Stripping Analyzer equipped with composite graphite mercury electrodes and a Charge Transfer Analyzer equipped with a mercury film electrode were

employed. The standard addition method was used to minimize the matrix effects of whole blood. The ASV results correlated well with those obtained by flameless atomic absorption analysis. The methods are simple, reliable, and suitable for applications in the clinical field. The procedure using the Charge Transfer Analyzer is recommended because of its sensitivity and rapidity.

Screening for Lead Absorption

C.R. Corum, L. Garcia, Jr., and J.D. Repko. OCCUP HEALTH SAF 1981 Mar;50(3):8-12.

Recent attention in occupational medicine to the neurological consequences of industrial lead exposure has led to the development of a method of partial antidromic blocking to determine the conduction velocity of the slower nerve fibers of the ulnar nerve. Since the slower conducting fibers of peripheral motor nerves are thought to be susceptible first to damage in neuropathies induced by absorption of lead, this technique appears to be appropriate for detecting subclinical nerve damage in individuals without clinical neurological symptoms. The described technique and equipment for neurological surveillance of workers could provide results conclusive enough to warrant removing an employee from a job.

University Conducts Lead Exposure Study

Anonymous. OCCUP HEALTH SAF 1981 Feb; 50(2):36-7.

The nervous system is particularly vulnerable to the toxic effects of certain heavy metals. In some industries, workers are unwittingly exposed for long periods of time before clinical manifestations are noted. Chronic low-level exposures may go unrecognized. The Department of Neurology at Boston University School of Medicine has detected subclinical damage among industrial workers and schoolchildren exposed to lead and other neurotoxins by using sensitive neurophysiological techniques that measure the speed at which an impulse travels along a nerve. A research team is conducting a case-control study among 112 workers at a lead foundry and a valve manufacturing company, which are located on the same grounds. Previous studies have found adverse physiologic, neurological, and psychological reactions among children and adults who had been exposed to even low doses of lead over a period of time in their homes or industrial environments. For example, behavioral disturbances were eight times more frequent in children exposed to lead than in children in a control group. These studies will contribute to the development of a protocol that could have broad application in the evaluation of occupational exposure to all neurotoxins.

Subclinical Effects of Chronic Increased Lead Absorption — A Prospective Study. III. Neurologic Findings at Followup Examination

G.H. Spivey, R.W. Baloh, C.P. Brown, B.L. Brody, D.S. Campion, J.L. Valentine, D.E. Morgan, and B.D. Culver. JOM 1980 Sep;22(9):607-12.

Authors' abstract: Neurologic examination, nerve conduction testing, and electro-oculographic testing have been performed at a baseline examination and a followup examination in a group of lead workers with blood lead levels predominantly between 60 and 80 μg/dl and in a group of control workers. A statistically significant decreased saccade accuracy measurement in the lead workers compared with the controls was found at both examinations. No other simple test or pattern of findings differentiated between the lead workers and the controls, and the biological significance of the lower saccade accuracy is not clear. Nerve conduction measurements do not appear to be a satisfactory method of detecting subclinical neurologic effects of lead exposure.

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EPIDEMIOLOGY

Areawide Chemical Contamination: Lessons from Case Histories

R.W. Miller. JAMA 1981 Apr 17;245(15): 1548-51.

Author's abstract: Nine case histories illustrate the mounting problems owing to chemical contamination that often extends beyond the workplace into the community. [One case history describes the absorption of lead in two young siblings who lived within 3 km of a large lead smeltery. Blood lead levels of the children were 68 and 81 mg/dl. Radiological examinations of their knees revealed characteristic lead lines.] The effects include not only carcinogenesis and teratogenesis, so much in the public's mind, but also severe neurological and gonadal disabilities immediately after exposure. Recognition of causal relationships is often made by astute clinicians. The experience of the Atomic Bomb Casualty Commission in studying Japanese survivors in Hiroshima and Nagasaki serves as a model for future studies of communities exposed to unusual environmental contamination.

Exposure to Lead by the Oral and the Pulmonary Routes of Children Living in the Vicinity of a Primary Lead Smelter

H.A. Roels, J.P. Buchet, R.R. Lauwerys, P. Bruaux, F. Claeys-Thoreau, A. Lafontaine, and G. Verduyn. ENVIRON RES 1980 Jun;22(1):81-94.

Authors' abstract: Yearly from 1974 to 1978, a medical survey was carried out among 11-year-old children attending schools situated less than 1 and 2.5 km from a lead smelter. Age-matched control children from a rural and urban area were examined at the same time. The blood lead levels (PbB) of the children living in the smelter area (mainly those attending schools located less than 1 km from the smelter) were higher than those of rural and urban children. The mean PbB levels were usually lower in girls than in boys, especially in the smelter area. Despite a slightly decreasing trend in the annual mean airborne lead (PbA) concentration at less than 1 km (mean PbA: from 3.8 $\mu g/m^3$ in 1974 to 2.3 $\mu g/m^3$ in 1978), the PbB levels there did not improve, whereas 2.5 km from the plant a significant tendency to normalization of PbB became apparent. Therefore, in the third survey, the medical examination was combined with an environmental study which demonstrated that lead in school-playground dust and in air strongly correlated. Lead on the children's hands (PbH) was also significantly related to lead in air or lead in dust. Less than 1 km from the factory boys and girls had on the average 436 and 244 μg Pb/hand, respectively, vs. 17.0 and 11.4 μg Pb/hand for rural boys and girls, respectively. Partial correlations between PbB, PbA, and PbH indicated that in the smelter area the quantitative contribution of PbA to the children's PbB is negligible compared with that of PbH. Thus, the control of airborne lead around the lead smelter is not sufficient to prevent excessive exposure of children to environmental lead. In view of the importance of lead transfer from dust and dirt via hands to the gastrointestinal tract, remedial actions should be directed simultaneously against the atmospheric emission of lead by the smelter and against the lead particulates deposited on soil, dust, and dirt.

Environmental Influences on Mouthing in Children with Lead Intoxication

N.A. Madden, D.C. Russo, and M.F. Cataldo. J PEDIATR PSYCHOL 1980 Jun;5(2):207-16.

Authors' abstract: The relationship of mouthing behavior to different environmental conditions was evaluated for three young children with asymptomatic lead poisoning. Specifically, the amount of mouthing; involvement with materials, adults, and other children; and noninvolvement were measured across daily sessions in three environments: group play, individual impoverished

play, and individual enriched play, using an interval-recording system. For each of the children, the results indicated that mouthing was exhibited significantly more in the impoverished setting as compared with either group play or individual enriched environments. The results suggested that simple environmental enrichment may hold promise in the reduction of mouthing and pica. Further research evaluating procedures for reduction of mouthing and pica is suggested.

Placental and Stillbirth Tissue Lead Concentrations in Occupationally Exposed Women

A.K. Khera, D.G. Wibberley, and J.G. Dathan. BR J IND MED 1980 Nov;37(4):394-6.

Authors' abstract: The lead values in maternal and infant blood, in placental tissue, and in stillbirth liver, kidney, and rib- and skull-bones have been determined in samples from the Stoke-on-Trent area. The lead values in antenatal blood and placenta increase with occupational exposure; liver and kidney stillbirth lead values are lower than those of much older children, and rib-bone lead values from stillbirths were on the average three times as high as those from a control group comprised of cot deaths and early infant deaths from accidental causes.

Occupational Exposure of Women to Inorganic Lead (Italian)

A. Cavalleri and F. Candura. MED LAV 1979 Sep-Oct;70(5):341-4.

English summary: The permissible limits for occupational exposure to lead have been the subject of ample discussion and reexamination in the last few years, but little attention has been given to the problem of the exposure of women in childbearing age and the consequences for the fetus. The fetus is an organism particularly sensitive to lead, to which it is exposed through the mother, since the metal easily passes the placental barrier. Since the level of lead in blood that is considered critical for the fetus is at values lower than those considered dangerous for the adult, the blood lead level of the mother should also be kept below this value. Attention is drawn to the necessity of regulatory action to deal with this problem, which appears to be of considerable importance in view of its health and social implications.

A Neurological and Biochemical Study of Early Lead Poisoning

J.A. Ashby. BR J IND MED 1980 May;37(2):133-40.

Author's abstract: Changes in nerve conduction velocity were found in 94 workers exposed to lead in a battery factory compared with 94 age-matched controls. There was no clinical evidence of nerve damage in the lead workers. The mean blood lead concentration in the 94 lead workers was 2.9 μmol/l (60 μg/100 ml), and their length of exposure to lead ranged from 6 months to 33 years. All mean maximum motor nerve conduction velocities (MMCV) measured were highly statistically significantly lower in the lead-exposed group compared with their age-matched controls. Thus mean ulnar MMCV was 53.4 m/s in lead workers and 55.6 m/s in control subjects ($p < 0.0005$); mean median MMCV was 55.9 m/s in lead workers and 57.3 m/s in control subjects ($p < 0.01$); mean radial MMCV was 63.9 m/s in lead workers and 71.1 m/s in control subjects ($p < 0.0005$); mean peroneal MMCV was 46.1 m/s in lead workers and 47.6 m/s in control subjects ($p < 0.005$). The amplitude of the muscle action potential produced by proximal stimulation of a nerve was expressed as a percentage of the amplitude of the muscle action potential produced by distal stimulation and the percentage amplitude thus obtained used as an indicator of the conduction velocity of slower fibers (SFCV). Peroneal nerve percentage amplitude of lead workers was statistically significantly lower ($p < 0.005$) than in the control group (means 86.6% and 90.3%, respectively). There were, however, no significant differences in the percentage amplitude in the ulnar and median nerves. It is suggested that percentage amplitude is an inappropriate indicator of SFCV in ulnar and median nerves. There was no statistically significant correlation to indicate that progressive slowing of nerve conduction (MMCV and SFCV) was associated with increasing exposure to lead (as indicated by blood and urine lead concentrations) or with the commonly measured biochemical changes associated with disturbed hemopoiesis in lead exposure (δ-aminolevulinic acid dehydrase; free erythrocyte protoporphyrin; hemoglobin and urinary δ-aminolevulinic acid). MMCV of the ulnar nerve was the only conduction velocity statistically significantly correlated with length of exposure to lead. Increased length of exposure to lead was associated with a decrease in the ulnar MMCV. Only 13 of the subjects had been exposed to lead for 2 years or less, and in none of them had the blood lead ever risen above 3.9 μmol/l (80 μg/100 ml) in 3 monthly tests (mean blood lead concentration at time of testing: 2.8 μmol/l). In these subjects the MMCV of ulnar, radial, and peroneal nerves and the peroneal percentage amplitude were statistically significantly reduced. The results from this group suggest that the onset of nerve conduction

changes occurs within 2 years and at concentrations of lead in blood of less than 3.9 μmol/l (80 μg/100 ml).

Assessment of Renal Function of Workers Exposed to Inorganic Lead, Cadmium or Mercury Vapor

J.P. Buchet, H. Roels, A. Bernard, and R. Lauwerys. JOM 1980 Nov;22(11):741-50.

Authors' abstract: The renal function of workers occupationally exposed to cadmium (n = 148), to mercury vapor (n = 63), or to inorganic lead (n = 25) has been compared with that of workers with no occupational exposure to heavy metals (n = 88). A moderate exposure to lead (Pb-B < 62 μg/100 ml) does not seem to alter renal function. Excessive exposure to cadmium increases the urinary excretion of both low- and high-molecular-weight proteins and of tubular enzymes. These changes are mainly observed in workers excreting more than 10 μg Cd/g creatinine or with Cd-B above 1 μg Cd/100 ml whole blood. Occupational exposure to mercury vapor induces glomerular dysfunction, as evidenced by an increased urinary excretion of high-molecular-weight proteins and a slightly increased prevalence of higher β_2-microglobulin concentration in plasma without concomitant change in urinary β_2-microglobulin concentration. β-galactosidase activity in blood and in urine is also increased. The likelihood of these findings is greater in workers with Hg-B and Hg-U exceeding 3 μg/100 ml whole blood and 50 μg/g creatinine, respectively. The hypothesis is put forward that the glomerular dysfunction induced by cadmium and mercury might result from an autoimmune mechanism.

Detection of Early Kidney Damage in Workers Exposed to Lead, Mercury, and Cadmium (German)

K.H. Schaller, J. Gonzales, J Thurauf, and R. Schiele. ZENTRALBL BAKTERIOL (B) 1980 Sep; 171(4-5):320-35.

English summary: Our study was performed to evaluate potential adverse effects on the kidney caused by an occupational exposure to cadmium, lead, and mercury, respectively. We examined 81 individuals from a Zn-Cd-plant and a Ni-Cd-battery factory occupationally exposed to cadmium. In a chemical company synthesizing mercury compounds, we analyzed 23 exposed workers. The 21 persons with an exposure to lead were employed in a secondary lead smelting plant. To evaluate the degree of the occupational exposure, we analyzed the concentrations of the heavy metals in blood and urine samples. As indicators of an adverse effect on the kidney, the renal elimination of specific proteins was determined. The analysis of proteins with a higher molecular weight, such as albumin and acid α_1-glycoprotein, was performed by using a newly developed laser nephelometric method. Patterns of renal-eliminated proteins with a lower molecular weight were characterized by applying a radioimmunological determination of β_2-microglobulin. The results found in workers exposed to cadmium verified previous studies. The occurrence of a characteristic β_2-microglobulinuria takes place after a sufficiently long period of exposure. In addition to this, cadmium-exposed workers had an increased elimination of total protein. Persons with an exposure to mercury also showed a slightly increased elimination of β_2-microglobulin and total protein. An intensive long exposure to mercury and its (in-)organic compounds seems to induce an increased renal elimination of proteins. No increased renal elimination was found in persons occupationally exposed to lead.

Erythrocyte Lead-Binding Protein after Occupational Exposure. I. Relationship to Lead Toxicity

S.R. Raghavan, B.D. Culver, and H.C. Gonick. ENVIRON RES 1980 Jun;22(1):264-70.

Authors' abstract: Lead content was determined in various fractions of red blood cell (RBC) hemolysates from normal controls and from three groups of lead-exposed workers: without toxicity, toxicity associated with high blood lead levels, and toxicity associated with low blood lead levels. The most significant finding was a decrease in the lead bound to a 10,000 molecular weight protein in the group of workers with toxicity at low blood lead levels (43 to 54 μg%). These results suggest that workers who have diminished capacity for synthesizing this low-molecular-weight lead-binding protein are at increased risk for developing lead toxicity at relatively low blood lead levels.

Epidemiological Study on the Relationships between Lead Exposure and Porphyrin Metabolism

A. Seubert, S. Seubert, L. Nottbohm, and H. Ippen. INT J BIOCHEM 1980;12(5-6):891-5.

Authors' summary: 5-Aminolevulinic acid dehydratase, erythrocyte porphyrins, blood lead, and urinary 5-aminolevulinic acid were determined in 53 patients not exposed to lead. A seasonally significant fall could be determined for 5-aminolevulinic dehydratase in the erythrocytes and for urinary 5-aminolevulinic acid. On the basis of the longitudinal study, it could be observed in persons with high lead exposure for the first time

that the individual bioparameters react to lead exposure in a different way. Whereas 5-aminolevulinic acid and porphyrins fall rapidly in the urine after ending exposure, blood lead and erythrocyte porphyrins remain raised over a long period. After renewed exposure, 5-aminolevulinic acid and blood lead remain in the industrial medically tolerable range, whereas the erythrocyte porphyrins rise markedly. The investigations on 314 lead workers show that values for blood lead, erythrocyte porphyrins, and urinary 5-aminolevulinic acid are in good agreement. The duration and intensity of the exposure do not have a large effect on the level of the values according to our results. Diurnal fluctuations in the bioparameters show marked variations of the urinary values, whereas blood lead and erythrocyte porphyrin values remain almost constant.

Genetic Effect of Low Doses of Radiation in Occupationally Exposed Workers in Coal Mines and in Coal-Fired Plants

D. Horvat, A. Bauman, and J. Racic. RADIAT ENVIRON BIOPHYS 1980;18(2):91-7.

Authors' abstract: Analyses of structural aberrations of chromosomes and of the body burden of lead-210 were carried out in a group of workers occupationally exposed to chemical pollutants and low doses of ionizing radiation during a technological process in which coal is used as fuel. A parallel study was performed in a control group of workers. In the exposed group the percentage of chromatid and chromosome aberrations and the results of radiochemical analyses were higher than in the control group.

Lead Levels in Human Lungs

E.M. Ophus and E.A. Mylius. BULL ENVIRON CONTAM TOXICOL 1977 Dec;18(6):734-41.

In this study, samples of lung tissue were obtained from autopsies on 250 individuals who died in Sor-Trondelag County, Norway, in the period 1974-76. Of the total, 139 were inhabitants of the city of Trondheim (population 120,000), and 111 were inhabitants of mainly rural areas. It was shown that the concentration of lead in the lungs of the urban group was significantly higher than in the rural group. Of the 250 individuals studied, 6 distinguished themselves as occupationally exposed. These six had a mean lead concentration in the lungs of 1.81 ppm dry weight, a lung lead level which was considerably higher than that found in any of the other lung tissue samples analyzed. Of the six occupationally exposed individuals (all males), three were employed in industry (factory and machine shop) and three were vehicle drivers. The relatively high content of lead in the lungs of the six men indicates that occupation is the most crucial parameter correlated with lung lead concentration.

Cigarette Smoking and Lead Levels in Occupationally Exposed Lead Workers

C.P. Brown, G.H. Spivey, J.L. Valentine, and B.L. Browdy. J TOXICOL ENVIRON HEALTH 1980 Jul;6(4):877-83.

Authors' abstract: One hundred and eleven workers at a secondary Pb smelter were surveyed to determine smoking and personal hygiene habits. Fifty-three percent of the smokers had blood Pb levels in excess of 60 μg/dl, compared with 31% of nonsmokers ($p = 0.02$). Among smokers, 66% of "heavy" smokers (those who smoked one pack or more cigarettes per day) had blood Pb levels over 60 μg/dl, compared with 39% of the "light" smokers ($p = 0.05$). Those who kept their cigarettes on their person had a higher proportion of blood Pb greater than 60 μg/dl than workers who kept their cigarettes elsewhere (63% versus 36%, respectively; $p = 0.08$). The difference in blood Pb levels between smokers and nonsmokers may be due in part to direct environmental contamination of cigarettes or impaired lung clearance mechanisms, and could be important in workers with already elevated blood Pb levels.

Blood-Lead and Cadmium in Human Hypertension

D.G. Beevers, J.K. Cruickshank, W.B. Yeoman, G.F. Carter, A. Goldberg, and M.R. Moore. J ENVIRON PATHOL TOXICOL 1980 Sep;4(2-3):251-60.

Authors' abstract: An epidemiological study among hypertensives and normotensives in Renfrew, Scotland, where drinking water hardness is very low (5 ppm) and water-lead levels are commonly high, has shown a significant association between high blood-lead levels and high blood pressure. No association was found with indices of renal function, plasma renin or angiotensin II concentrations, or serum uric acid levels. In a parallel study of blood-lead levels in Birmingham, England, where water hardness is low (20 ppm) but water-lead levels are also low, high blood-lead levels were not found, no relationship was found with blood pressure, and the prevalence of hypertension was lower than in Renfrew. We conclude that subclinical lead exposure from drinking water may be a factor in the development of hyperten-

sion. A study of blood-cadmium levels has shown no association between high blood pressure and subclinical cadmium exposure, but has confirmed a close relation between blood-cadmium and cigarette smoking. We conclude that previous reports of a cadmium-blood pressure link may be confounded by failure to allow for the cigarette smoking habits of the subjects studied.

Exposure to Trace Elements and Cardiovascular Disease

N.O. Borhani. CIRCULATION 1981 Jan;63 (1):260A-263A.

From author's summary: Perhaps among all trace elements implicated, the role of zinc, copper, cadmium and lead, individually or in combination, is more biologically plausible than others. There is, however, little evidence to make any definitive statement even on these elements, let alone draw any conclusion about their role in the pathogenesis of coronary heart disease. From a purely epidemiological point of view, the observations on the association between the levels of these trace elements and coronary heart disease lack strength and consistency. Further, these findings do not possess specificity and, in most instances, cannot be explained on the basis of a biologically plausible hypothesis. Thus, neither their association with the disease nor the mechanism of action of these trace elements in the pathogenesis of cardiovascular diseases, especially coronary heart disease, is determined at present. There is an urgent need to design and conduct, perhaps in a national collaborative manner, a prospective epidemiological study aimed at delineating the possible influence of trace elements in the incidence of cardiovascular diseases and coronary heart disease. The future direction of research efforts will depend on the consistent demonstration of a dose-effect relationship between trace elements and specific cardiovascular diseases. It is important that further research in this field include autopsy and clinical studies of special groups of patients selected to maximize environmental exposure effects and minimize, or control for, effects of established disease or genetic influences. Additionally, there is an important need for further basic investigation of the role of trace elements in metabolic and regulatory processes. Clinical, epidemiological, and laboratory research hold considerable promise.

Blood Lead Concentrations in a Remote Himalayan Population

S. Piomelli, L. Corash, M.B. Corash, C. Seaman, P. Mushak, B. Glover, and R. Padgett. SCIENCE 1980 Dec;210(4474):1135-7.

Authors' abstract: The lead content in the air at the foothills of the Himalayas in Nepal was found to be negligible. The concentration of lead in the blood of 103 children and adults living in this region was found to average 3.4 μg/dl, a level substantially lower than that found in industrialized populations.

Public Health Aspects of Toxic Heavy Metals in Animal Feeds

R.P. Sharma and J.C. Street. J AM VET MED ASSOC 1980 Jul 15;177(2):149-53.

Authors' abstract: Studies involving animals of three species (dairy cattle, growing swine, and laying chickens) indicated that residues of lead and cadmium do not increase appreciably in major food products obtained from the animals during long-term exposure to subtoxic dietary concentrations of these heavy metals. Human risk would not be expected by the consumption of milk, meat, or eggs from animals similarly exposed. Both metals accumulate in liver and kidney, and lead accumulates in bone. A moderate intake of liver and kidney from lead-exposed animals appears to present little or no health hazard. Utilization of these organs from cadmium-exposed animals, however, should be avoided.

Lead Modelling—A Decision-Making Tool

J.E. McEvoy. SCI TOTAL ENVIRON 1980 Dec;16(3):231-7.

Author's abstract: The difficulties of decision-making in a state of ignorance regarding the problem area, [a situation which is] true for many questions of environmental pollution, are discussed with reference to lead. Before irrevocably committing a considerable amount of both capital and material resources, the policy-maker would like to make a prediction about the potential effectiveness of any control measure. To this end, a mathematical model is suggested which represents the transport of lead within a standard man. It may be used at two discrete levels, either to analyze a number of control strategies in terms of their relative effectiveness in reducing blood lead concentrations, or, dependent upon the model's accuracy and the availability of data concerning the exposure to, and metabolism of, lead by a specific population, to select between two or more directly competing strategies for the control of that population's lead exposure, the selection of the optimum strategy being based on the model's output. Modelling may be seen, therefore, to satisfy, at least in part, the need for decision-making information in an area where time may not permit the acquisition of appropriate, unequivocal scientific evidence.

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RESEARCH AND EVALUATION

Toxicity, Mutagenicity, and Teratogenicity of Lead

G.B. Gerber, A. Leonard, and P. Jacquet. MUTAT RES 1980 Sep;76(2):115-41.

Authors' summary: Environmental contamination by lead has greatly increased as more and more lead is used for gasoline and in various industrial products, although severe cases of lead intoxication, as often seen in former times, have become rare owing to better health care. These facts have drawn attention to effects of lead which may arise, possibly without a threshold, at low exposure levels. Among the classical manifestations of lead intoxication are anemia and gastrointestinal, renal, and nervous symptoms. Those in the nervous system and perhaps also in the kidney may have consequences even at subclinical levels of lead exposure. Thus, the possibility that such exposure may cause mental alterations in children, induce late renal damage, or affect nerve conduction is now much debated. The mechanisms of action of lead on the developing central nervous system are still uncertain. They may be related to a composition between lead and calcium on the synaptosomal level. Among the typical stochastic risks, tumors have been found in lead-intoxicated rodents, but do not seem to occur in man, and the situation with respect to genetic risks is not entirely clear. Certain effects of lead on genetic material have been observed in simple organisms, and it appears that lead exposure in vivo or in vitro can induce light chromosomal aberrations such as gaps and fragments. Under conditions of calcium deficiency, severe aberrations such as dicentrics may also arise; but the data on man are controversial because lead is almost never the only potentially mutagenic agent to which people are exposed in an industrial environment. Nevertheless, the efficiency of lead in causing such aberrations appears low compared with that of other mutagenic agents so that genetic effects of lead do not appear of primary concern for human health. Lead can prevent implantation of the embryo, delay its growth during later stages of pregnancy and, when injected during organogenesis particularly under conditions of calcium deficiency, cause malformations. The risks to the developing human organism are difficult to evaluate owing to the large differences in lead metabolism between man and rodent, so studies on species resembling man are desirable.

Prenatal and Neonatal Toxicology and Pathology of Heavy Metals

L.W. Chang, P.R. Wade, J.G. Pounds, and K.R. Reuhl. ADV PHARMACOL CHEMOTHER 1980;17:195-231.

The adverse effects of lead on the reproductive system have been well documented. The developing organism is especially sensitive to lead poisoning. The harmful effects of lead on the fertility and reproduction of humans as a result of occupational exposure have long been recognized. Lead readily crosses the placenta, producing an increase in blood lead levels in the fetus. Mammary transfer may pose a significant source of lead to newborns; in addition, the intestinal absorption of lead may be greatly enhanced by milk. The importance of lead as a human teratogen has not been established, although spontaneous abortion in human patients as a result of high lead exposure has been reported. Evidence for these effects has been borne out by studies in rats, mice, hamsters, and other animal models. Similar results and studies are discussed for mercury and cadmium. The phenomena of metal-metal interaction and metal-element interaction within maternal and fetal systems make the overall understanding of metal toxicology more complex. Metal-induced teratology represents one of the most important areas in toxicology.

Immunotoxicology of Heavy Metals

L.D. Koller. INT J IMMUNOPHARMACOL 1980;2(4):269-79.

From author's conclusions: From data which have been accumulated, lead appears to consistently suppress most of the segments of the immune system, while cadmium has produced mixed reactions. Mercury suppresses the primary humoral immune response, while selenium enhances humoral immunity. Zinc deficiency results in atrophy of the thymus with subsequent reduction in the humoral immune capacity. Nickel deters many segments of the immune response. Many of the other metals also compromise various parts of the immune system.

This review is certainly not complete, but [it] has compiled considerable data to document the adverse effects of metals on the immune response of experimental animals. Many of these immunosuppressive features are unaccompanied by clinical signs of disease. Therefore, it is apparent that many metals are detrimental to health by mechanisms other than direct toxicity. A chemical that impairs or destroys any portion of the immune system usually limits the defense mechanism of a host to infectious agents, thereby potentiating pathogenicity of that organism. A host that is rendered increasingly susceptible to an infectious agent is likely to develop complications or succumb to what normally would be a nonfatal condition.

Behavioral Effects of Moderate Lead Exposure in Children and Animal Models: Part 1, Clinical Studies

R. Bornschein, D. Pearson, and L. Reiter. CRC CRIT REV TOXICOL 1980;8(1):43-99.

From authors' conclusions and recommendations: A total of 22 studies were reviewed which addressed the question of the effects of moderate lead exposure on the behavioral development of children. There was no clear trend indicating that moderate lead exposure caused any abnormalities in behavioral development in children, nor was there any compelling evidence which suggested that this was not the case. A further complication with respect to these studies is that many of them had methodological deficiencies which undermined the credibility of their results. The findings from all 22 studies appear to be contradictory and do not offer any resolution to the question of whether moderate lead exposure is a significant health hazard. The data reviewed do not permit unequivocal determination of the level at which lead exposure begins to constitute a significant health hazard, as reflected in impaired neurobehavioral development. The ideal course that needs to be taken in this area of research is to prospectively monitor lead exposure and behavioral development in large samples of children. Careful and persistent monitoring of lead exposure should enable the investigators to more appropriately approach the controversial question of whether moderate lead exposure affects behavioral development in children. Careful attention needs to be paid to developing and using a number of tests to tap discrete behavioral functions that mediate intellectual and social behavior. A rigorous neuropsychological approach to assessing behavioral functions should be adopted in studies as the best way of ensuring measurement of areas of skill where deficits due to moderate lead exposure are likely to occur. A final recommendation would be for investigators to adopt multivariate research designs in approaching the study of this problem.

Behavioral Effects of Moderate Lead Exposure in Children and Animal Models: Part 2, Animal Studies

R. Bornschein, D. Pearson, and L. Reiter. CRC CRIT REV TOXICOL 1980;8(2):101-52.

From authors' critique: Clarification of the nature of the interaction between lead and behavior has been sought through the use of animal models. Unfortunately, much of the data generated by these animal studies are of little use due to inappropriate exposure levels or the lack of control over, and systematic variation of, critical independent variables known or suspected to interact with lead. However, one of the most damaging aspects of these animal studies has been a lack of a clinical perspective, both in the definition of the critical issues and in the design of studies to deal with these issues. Few animal studies adequately simulate the lead exposure conditions found in young children, either with respect to the levels of exposure or the timing of the exposure. There is often an inadequate or nonexistent history of lead exposure with respect to both the external and internal dose. Correlative measures of lead toxicity in other target systems, e.g., hematopoietic or renal indices, are generally absent. This makes it impossible to assess accurately the relative sensitivity of the major target organ systems in the lead-exposed animal. The present data do not permit us to distinguish clearly between the effects of lead exposure on cognitive function (learning/memory) and effects on sensory-motor function, arousal, or motivation, which in turn can produce performance differences. Relevance of these animal data to the clinical situation and ease of interpretation of data can be increased in future studies by consideration of the following: (1) Better documentation of internal dosage levels is needed. Blood and tissue lead levels during exposure and at the time of testing are necessary. (2) Use of exposure protocols

which do not produce growth retardation or the use of experimental designs which permit an evaluation of the nature of the interaction between level of lead exposure and degree of growth retardation should be encouraged. (3) Increased numbers of litters should be included in each treatment group in order to reduce the contribution made by "litter effects." A second alternative would be to use a genetically more homogeneous test population. (4) Standard reference compounds (positive controls) or environmental manipulations which permit an evaluation of test sensitivity should be incorporated into the experimental design. (5) Inclusion of correlative indices of lead toxicity, e.g., free erythrocyte protoporphyrin levels in blood or ALA in the urine, would aid in the extrapolation of animal data to humans.

Concentrations of Lead in the Tissues of Children

P.S. Barry. BR J IND MED 1981 Feb;38 (1):61-71.

Author's abstract: Twenty-four different tissues from 73 children and infants, including stillbirths, were analyzed for lead content. In the youngest group of 49 infants aged under 1 year, including 14 stillbirths, the mean concentrations of lead in their soft tissues were all less than 0.3 ppm and nearly all were less than the concentrations found in the soft tissues of older children or of adults. The mean concentrations of lead in the bones in the infant group were greater than in their soft tissues, but still less than 1 ppm, and were 10-40 times less than in bones of adults and about 3 times less than in the bones of older children. Lower concentrations of lead were observed in the tissues of stillbirths than in those of neonatal live births, at a 95% level of significance by analysis of variance. In 24 children aged 1-16 there was no clear evidence of increase of lead concentrations in the bones with increasing age; neither was there evidence of a difference in the concentrations of lead in types of bone. Although the mean concentrations in the bones were greater in the children aged 1-16 than in those of infants aged under 1 year, the data did not suggest that a progressive accumulation of lead occurred in the bones, [until] probably [at about] the end of the second decade of life, by which time the growing phase will be nearing completion. In 18 children aged 1-9 and in 6 children aged 11-16 the concentrations of lead in the soft tissues were similar, and comparable with those observed in women. The ratio differences between ash-weight and wet-weight measurement in the different types of bone in children did not differ proportionately from the adult ratios, suggesting a similarity in the patterns of deposition of lead in bone, irrespective of age. No differences in tissue lead concentrations by sex were observed in the infant group of children, or when the concentrations in the tissues were related to the years in which the samples were obtained. Individual tissues showed different concentrations and patterns of distribution of lead, which were skewed more towards low values in the infant group than in older children. The results of other studies, of which there have not been many, were found to be in general agreement with those reported here. The exposure of infants to lead appeared to be less than in older children or in adults, probably for reasons associated with lack of availability and parental care.

In Vivo Determination of Lead in the Skeleton after Occupational Exposure to Lead

L. Ahlgren, B. Haeger-Aronsen, S. Mattsson, and A. Schutz. BR J IND MED 1980 May;37(2): 109-13.

Authors' abstract: The concentrations of lead in the phalanges and in the blood were determined in 22 subjects who had formerly been exposed to lead in a storage battery plant, which had been closed for 7 years. The bone lead concentration was measured in vivo by using an X-ray fluorescence technique in which two ^{57}Co γ-ray sources were used for generating the characteristic X-rays of lead, which were measured with a Ge(Li) detector. In three subjects the variation of the lead concentration along the forefinger was measured together with the lead concentration in the tibia. The measured lead concentrations in the phalanges were between 20 μg/g (our detection limit) and 118 μg/g. The lead concentration in the phalanges was found to increase with the length of employment, but no simple relation was found between the lead concentrations in the blood and in the phalanges. The decrease in the blood lead concentration after the cessation of exposure was followed in four subjects. Seven years after exposure had ended, the blood lead concentration was found to be more dependent on the daily intake of lead than on the release of lead from the skeleton. These experimental results could be explained by a two-compartment model using exchange rates given in publications. This model has also been used to calculate the blood lead concentration that could be achieved after a sudden release of lead from the skeleton.

The Distribution of Lead in Human Teeth, Using Charged Particle Activation Analysis

T. Al-Naimi, M.I. Edmonds, and J.H. Fremlin. PHYS MED BIOL 1980 Jul;25(4):719-26.

Authors' abstract: A technique has been developed to measure lead content in teeth by using $^{3}He^{2+}$ activation analysis. The α-activity produced in the teeth is recorded on plastic film alpha-track detectors (LR-115) and compared with the activity produced by the lead contained in standard glass. The concentration in teeth from three areas of the United Kingdom has been determined as a function of age. The lead content is found to increase with age in dentine and pulpal dentine, but not in enamel.

A Nuclear Microprobe Investigation of Heavy Metal Distribution in Individual Osteons of Human Femur

U Lindh. INT J APPL RADIAT ISOT 1980 Dec; 31(12):737-46.

Author's abstract: The analytical capacity of charged-particle induced interactions for assessment of multi-element distributions in mineralized tissue was explored in autopsy sections of human femur. The PIXE [particle-induced X-ray emission spectroscopy] technique was employed in a nuclear microprobe with 2.5 MeV protons. Comparison of the standard method approach and the direct utilization of analytical formulae was performed. Detection limits of a few ppm were attained for some elements, and the positional resolution was 20 μm. The analytical errors did not exceed 15%. Concentration gradients of lead and zinc resulting from occupational exposure were clearly established within individual osteons of the femur.

Role of Altered Heme Synthesis in Lead Neurotoxicity

E.K. Silbergeld and J.M. Lamon. JOM 1980 Oct;22(10):680-4.

Authors' conclusions: The effects of lead on heme synthesis can be associated with the accumulation of possibly neuroactive precursors or depletion of heme for nonhemoglobin metabolism, or both. These consequences provide support for the following conclusions: (1) Increased aminolevulinic acid (ALA) associated with lead exposure may represent not only an accessible indicator of lead exposure, but also the presence of increased production of a potential neurotoxin; (2) The inhibition of heme synthesis produced by lead may have functional significance for heme-dependent processes (hemoproteins) other than red cell hemoglobin; (3) The relationship of lead absorption, or of tissue lead concentrations, to these phenomena is unclear and requires further research; (4) The possibility that altered heme metabolism may be responsible for the neurotoxic manifestations of lead poisoning may provide an explanation of the well-described neurological similarities between lead poisoning and the acute attack forms of porphyria.

High Affinity of Lead for Fetal Hemoglobin

C.N. Ong and W.R. Lee. BR J IND MED 1980 Aug;37(3):292-8.

Authors' abstract: In vitro experiments using ^{203}Pb were performed to identify lead-binding components in human hemoglobin. Sephadex A-50 ion-exchange chromatography of hemolysate showed that different types of hemoglobin had different affinities for lead. For the hemolysate from adults, lead was present in both Hb A (α_2 β_2)and HB A_2 (α_2 δ_2). In the hemolysate from newborn infants, the hemoglobin of fetal origin, Hb F (α_2 γ_2), showed a much greater affinity for ^{203}Pb than the adult hemoglobin, Hb A (α_2 β_2), obtained from maternal blood. Analysis of the ^{203}Pb-labelled hemoglobin suggested that about 82% of ^{203}Pb was in the globin polypeptide. Further analysis with carboxylmethyl (CM) cellulose chromatography indicated that the γ globin of fetal origin had a higher affinity for ^{203}Pb than the β globin, whereas α globin appeared to be unimportant in lead binding. The results of the different affinities for lead of different Hb types are discussed with regard to the effect of lead upon hemoglobin synthesis.

Simultaneous Quantitation of Zinc Protoporphyrin and Free Protoporphyrin in Erythrocytes by Acetone Extraction

D. Hart and S. Piomelli. CLIN CHEM 1981 Feb;27(2):220-2.

Authors' abstract: Erythrocyte protoporphyrin content is increased in several human and veterinary disorders in which heme synthesis is disrupted. The nature of the defect determines whether zinc protoporphyrin, or unchelated (free) protoporphyrin, or both, are present in the erythrocytes. Extraction of the protoporphyrin into acetone/water (80/20 by vol) is a simple, rapid technique by which each protoporphyrin species is delivered into solution without zinc being removed from zinc protoporphyrin. The ratio of zinc protoporphyrin to total protoporphyrin concentration correlated significantly with the ratio of fluorescence emission intensities at the zinc protoporphyrin peak and at an isosbestic point. This concentration ratio may be used with a quantitative measure of total erythrocyte protoporphyrin to define the absolute zinc protoporphyrin and free protoporphyrin content of erythrocytes.

Quantitative Assay of Erythrocyte "Free" and Zinc-Protoporphyrin: Clinical and Genetic Studies

S. Schwartz, B. Stephenson, D. Sarkar, H. Freyholtz, and G. Ruth. INT J BIOCHEM 1980; 12(5-6):1053-7.

Authors' summary: An improved extraction procedure and two fluorimetric techniques have been developed for the quantitative assay of "free" and Zn-protoporphyrin in circulating erythrocytes. Sources of error (including nonspecific fluorescence and diminished fluorescence due to absorbance of exciting light) can be essentially eliminated, especially through analysis of second derivative fluorescence spectra. As an alternative, the content of the two forms of protoporphyrin can be determined by noting the magnitude and relative intensity of fluorescence before and after acidification to remove any bound zinc. The concentration of "free" protoporphyrin was elevated specifically in acute Pb poisoning, in bovine (heterozygous) carriers of the protoporphyria trait, and in groups of renal patients undergoing dialysis. Many of the latter also showed appreciable amounts of Zn-coproporphyrin. Though the "free" protoporphyrin comprised an average of only 7%-10% of the total in normal humans, it usually constituted 25% or more of the total in normal cows, rats, rabbits, and dogs.

New Method for Liquid-Chromatographic Measurement of Erythrocyte Protoporphyrin and Coproporphyrin

M. Salmi and R. Tenhunen. CLIN CHEM 1980 Dec;26(13):1832-5.

Authors' abstract: We describe a "high-pressure" liquid-chromatographic method for separating all the porphyrins in the heme biosynthetic pathway. The preliminary extraction and purification method is such that only erythrocyte porphyrins with fewer than five carboxyl groups, which include protoporphyrin and the much smaller amount of coproporphyrin present, are measured. The porphyrins extracted from erythrocytes are chromatographically separated by use of a simple eluent system and fluorometrically detected.

"Ultra-Clean" Isotope Dilution/Mass Spectrometric Analyses for Lead in Human Blood Plasma Indicate That Most Reported Values Are Artificially High

J. Everson and C.C. Patterson. CLIN CHEM 1980 Oct;26(11):1603-7.

Authors' abstract: We measured lead concentrations in venous blood plasma from two subjects, one having a typical exposure and the other a high exposure to lead. Our preliminary data, obtained by isotope dilution/mass spectrometric techniques in an ultra-clean laboratory, show lead concentrations of 0.02 μg/l and 2 μg/l, respectively, in their blood plasma, and 110 μg/l and 800 μg/l, respectively, in samples of whole blood. These results indicate that plasma lead concentrations previously reported have been overestimated by a large factor and that further improvements in analytical procedures are needed in most laboratories before data on lead concentrations in blood plasma can be properly interpreted. Our preliminary data indicate a positive correlation between lead intake and lead concentrations in blood plasma.

Lead in Bone. I. Direct Analysis for Lead in Milligram Quantities of Bone Ash by Graphite Furnace Atomic Absorption Spectroscopy

L.E. Wittmers, Jr., A. Alich, and A.C. Aufderheide. AM J CLIN PATHOL 1981 Jan;75(1):80-5.

Authors' abstract: A method for direct lead content analysis of milligram quantities of bone ash by flameless atomic absorption spectroscopy is described. Bone ash (25 mg) is dissolved with HNO_3 and diluted with H_2O and La_2O_3 (1,000 μg/ml) solution. Lanthanum ion is used to suppress matrix interferences possibly arising in part from sulfate components of the bone ash. Two bulk bone samples (about 14 and 60 μg Pb/g ash, respectively) were used to determine daily, within-day, and overall variability of the method. Values for "low lead" bone samples were 14.08 $\pm$ 1.74 (SD) μg Pb/g ash and for "high lead" bone samples were 60.85 $\pm$ 5.24 (SD) μg Pb/g ash. The overall value of 58 lead recovery determinations from bone ash analysis was 103.5% $\pm$ 12.9% (SD). These values compare favorably with results previously reported for gram amounts of sample.

Abnormal Distribution of Lead in Amyotrophic Lateral Sclerosis—Reestimation of Lead in the Cerebrospinal Fluid

S. Conradi, L.O. Ronnevi, G. Nise, and O. Vesterberg. J NEUROL SCI 1980 Dec;48(3):413-8.

Authors' abstract: The lead concentration in CSF [cerebrospinal fluid] was determined by flameless atomic absorption spectrophotometry in 16 ALS [amyotrophic lateral sclerosis] patients and 22 control cases. The mean values were 0.69

± 0.55 (ALS) and 0.41 ± 0.37 (controls), $p < 0.01$. This confirms our earlier findings of raised CSF lead levels in ALS, but the present values are lower than previously reported for both ALS patients and controls.

The Percutaneous Absorption of Lead-203 in Humans from Cosmetic Preparations Containing Lead Acetate, as Assessed by Whole-Body Counting and Other Techniques

M.R. Moore, P.A. Meredith, W.S. Watson, D.J. Sumner, M.K. Taylor, and A. Goldberg. FOOD COSMET TOXICOL 1980 Aug;18(4):399-405.

Authors' abstract: The percutaneous absorption of lead from two hair-darkening cosmetic preparations containing lead acetate has been measured by radioisotopic tracer techniques, using lead-203 acetate, in eight normal human male subjects. Spiked preparations were applied in fluid and dried forms to each subject's forehead (with periods of 1 month between each application). The quantity of lead absorbed was calculated from blood counts, whole-body counts, and urine radioactivity. Results were normalized for each subject by administration of an IV tracer dose of lead-203 chloride, from which absorption was calculated. It was found that absorption of lead through the skin was essentially zero, with results ranging between 0 and 0.3% of the dose applied to whole skin. Slight absorption was found when the skin was broken. The potential hazard of the use of such cosmetic preparations is therefore considered to be insignificant.

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